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Docket No. G-085US04CON

Serial No. 09/818,260

In the Claims

1. (Previously Presented) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

- a) obtaining haplotypes for all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining haplotypes for all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;
- d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance.

2-3. (Canceled)

4. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising an input device and:

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(a) first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;

(b) second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(c) third instructions for determining the sum of separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(d) fourth instructions for determining the difference of said sum and said combined likelihood; and

(e) fifth instructions for determining the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance;

wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices.

5-6. (Canceled)

7. (Previously Presented) A programmed storage device comprising instructions that when executed perform a method comprising:

(a) determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately; and

(b) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (a) to determine the probability that the groups of (a) do not come from the same distribution of haplotypes.

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8-39. (Canceled)

40. (Previously Presented) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

- a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;
- d) calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype; and
- e) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance.

41. (Previously Presented) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

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- a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;
- d) assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype; and

c) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of step (a) and step (b) to determine the probability that the groups of step (a) and step (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance.

42-45. (Canceled)

46. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising an input device and:

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(a) first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;

(b) second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(c) third instructions for determining the sum of separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

(d) fourth instructions for determining the difference of said sum and said combined likelihood; and

(e) fifth instructions for calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype; and

(f) sixth instructions for determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups of (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance;

wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices.

47. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising an input device and:

first instructions for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;

second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

third instructions for determining the sum of the separate likelihoods that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary

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code;

fourth instructions for determining the difference of said sum and said combined likelihood;  
and

fifth instructions for calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype; and

sixth instructions for determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (b) to determine the probability that the groups of (b) do not come from the same distribution of haplotypes and assessing the statistical significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance;

wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices.

48. (Previously Presented) A programmed storage device comprising instructions that when executed perform a method comprising:

(a) determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

(b) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (a) to determine the probability that the groups do not come from the same distribution of haplotypes; and

(c) calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype.

49. (Previously Presented) A programmed storage device comprising instructions that when executed perform a method comprising:

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(a) determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

(b) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups of (a) to determine the probability that the groups do not come from the same distribution of haplotypes; and

(c) calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype.

50. (Previously Presented) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising:

a) obtaining haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;

b) obtaining haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;

c) identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;

d) using said binary mask array for analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

1) determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

2) determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

3) determining the difference of said sum and said combined likelihood; and

4) determining the significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between the groups of (d)(1) and (d)(2) to determine the probability that the groups of (d)(1) and (d)(2) do not come from the same distribution of haplotypes and assessing the statistical

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significance of the difference of said sum and said combined likelihood based on the probability that the test value could have resulted purely by chance.

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